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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,375	05/10/2005	Yuman Fong	08582/014002	5371
21559	7590	07/24/2007		
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			EXAMINER HAMA, JOANNE	
			ART UNIT 1632	PAPER NUMBER
			MAIL DATE 07/24/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/505,375	<b>Applicant(s)</b> FONG ET AL.	
	<b>Examiner</b> Joanne Hama, Ph.D.	<b>Art Unit</b> 1632	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 May 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3-14,22,23 and 28 is/are pending in the application.
- 4a) Of the above claim(s) 14,22 and 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-13 and 28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

Applicant filed a response to the Non-Final Action of February 12, 2007 on May 14, 2007. Claims 1, 28 are amended. Claims 14, 22, 23 are withdrawn.

Claims 1, 3-13, 28 are under consideration.

Applicant requests that rejoinder of claims 14, 22, 23 to be reconsidered.

Applicant indicates that the claims of Group 1 and 2 define a technical feature linking the inventions of these groups, which defines a contribution of US 2002/0071832 and that this will be discussed in more detail in connection with the rejections based on the cited reference, over which the present invention is novel and inventive (Applicant's response, page 5, under "Remarks"). In response, nothing in Applicant's response indicates what of the present invention is novel and inventive such that Groups 1 and 2 should be combined. In addition to this, the Lack of Unity/Restriction Requirement of October 12, 2005, page 4, indicated that the groups were separated because the two groups lacked a special technical feature: group 1's special technical feature being a surgically resected tumor and group 2's special technical feature being administration of virus prior to excision of the tumor. Further, art (US 2002/0071832) teaches administration of replication competent herpes virus into a resected tumor bed to ensure destruction of any remaining tumor cells, such that the claimed invention is not novel over the prior art. Thus, the groups remain separated.

This application contains claims 14, 22, 23, drawn to an invention nonelected with traverse in the reply filed on November 17, 2005. A complete reply to the final

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rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

**Maintained Rejections**

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 6, 8-13 remain rejected under 35 U.S.C. 102(e) as being anticipated by Fong et al., US 2002/0071832, for reasons of record, December 28, 2005, July 7, 2006, and February 12, 2007.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Applicant's arguments filed May 14, 2007 have been fully considered but they are not persuasive.

Applicant indicates that the specification provides support for the amendments to claims 1 and 23 and indicates that the specification indicates that the method of the invention is to treat primary tumors as well as to prevent lymphatic metastases and that the method follows the same pathways as metastasizing tumor cells, thus enhancing the likelihood of (the virus) reaching those areas within in the lymphatic system, e.g. lymph nodes (Applicant's emphasis, Applicant's response, page 6). Applicant indicates that Fong does not teach treatment of subjects such as those now specified in the present claims, which are in need of treatment of cancer at a site distal to the site of surgical resection of a tumor. Rather, Fong suggests inoculation of viruses into a resected tumor bed to destroy tumor cells remaining in the tumor bed and that the methods of the present invention are not inherent in the method of Fong (Applicant's response, page 7, 2<sup>nd</sup> parag.). Applicant also indicates that in the event that the Examiner considers the present subjects to be a species of the genus of cancer patients, Applicant submits that a genus does not anticipate a species (Applicant's response, page 7, 3<sup>rd</sup> parag.). In response, Applicant's amendment is not persuasive. The newly inserted phrase, "wherein said subject is in need of such treatment," in claim 1, is still readable as generic for a cancer patient who has metastases and is not limited to lymphatic metastasis. Applicant indicates that the specification points out a particular additional benefit of the claimed invention, i.e. that it prevents lymphatic metastases (Applicant's response, page 6; 2<sup>nd</sup> citation from the specification (i.e., specification, page 2, lines 25-30)). While the specification may indicate this particular benefit; claim 1 is not limited to patients who have lymphatic metastases.

Applicant indicates that the method of Fong was not taught to be carried out with the subjects specified in the present claims and thus, the presently claimed method provides a new approach for treating subjects as noted above (e.g. subjects with tumors found to have metastasized or having a high propensity to metastasize) and that there is no issue as to enablement of claim 1 (Applicant's response, page 8, 2<sup>nd</sup> parag.). In response, Applicant's amendment of adding the phrase, "wherein said subject is in need of such treatment," to claim 1 does not overcome the rejections at hand as the claims remain broad for any metastatic cancer and that the Fong et al. teach a method that can be used in a cancer patient who needs treatment.

With regard to the Examiner quoting page 10 of the specification, "this study investigates the use of an attenuated, replication-competent, oncolytic herpes simplex virus (NV1023), both to treat a primary tumor by direct injection, and to travel through the lymphatic system to treat metastatic tumors within the lymph nodes draining lymph from the site of primary cancer," Applicant indicates that when read in context, two separate methods are being described: i) direct tumor injection, and ii) administration resulting in travel through the lymphatic system (Applicant's response, page 8, 4<sup>th</sup> parag. to page 9, 1<sup>st</sup> parag.). In response, the point the Examiner was making with regard to the quotation of page 10 of the specification was that the specification teaches that administration of virus at the site of resection (specification, page 12, lines 14-15) is the same step as that taught by Fong et al., page 5, 2<sup>nd</sup> col. parag. 36. While Fong et al. do not specifically disclose that the virus administered at the site of resection can

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treat metastatic cancer, the ability for it to do so is inherent as the steps between Fong et al. and the claims are the same.

Applicant indicates that it was not stated that it is not effective to focus only on the site of excision as the site of administration, but rather, based on the prior art, administration to such a site would not have been considered to be effective for the treatment of metastases, and thus would not have been used with the patients now specified in the claims (Applicant's response, page 9, 2<sup>nd</sup> parag.). In response, this is not persuasive because regardless whether the prior art realized that administration at the site of resection would or would not be effective in treating metastatic cancer, the method step of administering virus at the site of resection was disclosed in the prior art and would have inherently had the ability to treat metastatic cancer.

Applicant provides a clarification of the issue of Fong's statement concerning the administration of virus to surgical beds that the type of cell targeted is a cell that has the potential to grow at the site of the surgical bed, and not cells that may have already traveled from the surgical bed. Applicant indicates that Fong's statement that the method is carried out to "ensure destruction of any remaining tumor cells" (i.e., cells remaining at the tumor bed) is reasonable because most cells in a tumor do not have metastatic potential (as supported in the prior Reply and prior cited references).

Applicant indicates that it was not until the present invention that it became known that cells already traveling from the resection site, such as through the lymphatic system can be targeted by administration to a surgical bed. In response, this is not persuasive. As indicated above, while the prior art was unaware that the method step of administering

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virus to the site of resection could be used to treat metastatic cells, the claimed method step of administering at the site of resection is anticipated in the prior art and treatment of metastatic cells would have been inherent.

Applicant indicates that the in vivo experiments of treating a mouse model of cancer, using OCUM-2MD3 metastatic cells, treated mice intraperitoneally and not at a surgical bed (Applicant's response, page 10, 1<sup>st</sup> parag.). In response, Fong et al. teach the claimed method steps of dissection of the tumor and administration of virus at the site of the resected tumor (Fong et al., page 5, 2<sup>nd</sup> col., parag. 36), and thus, these steps anticipate the claims. The Examiner viewed Fong et al.'s working example to determine that Fong et al. had support for the general method described on page 5. The Examiner had interpreted the working example as an indicator that, virus and chemotherapeutic agent in the vicinity of the cancer could be used to treat metastatic cancer. Finally, as indicated in the Office Action, February 12, 2007, pages 9-10, it is noted that the phrase, "treating metastasis," is broad and in addition to ablating distant sites of cancer, "treating" could also mean "preventing" metastasis. It is noted that Fong et al. indicates that virus can be added to the resected site to ensure destruction of any remaining tumor cells (Fong et al., page 5, 2<sup>nd</sup> col., parag. 36) which may metastasize.

Thus, the claims remain rejected.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:



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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 6, 7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Fong et al., US 2002/0071832 in view of Wong et al., 2001, Human Gene Therapy, 12: 253-265, for reasons of record, December 28, 2005, July 7, 2006, and February 12, 2007.

Applicant's arguments filed May 14, 2007 have been fully considered but they are not persuasive.

Applicant indicates that the instant claims have been amended to specify the treatment of subjects in need of treatment of metastasis of cancer at a site distal to the site of surgical resection of a tumor and that Fong does not teach the treatment of such subjects (Applicant's response, page 10, 2<sup>nd</sup> parag. under "Rejections under 35 U.S.C. § 103(a)"). In response, as discussed above, Fong et al. teaches the same steps as those recited in the claims. As such, Fong et al. anticipates the claimed invention. Applicant indicates that the focus of Fong is the destruction of tumor cells at the site of resection. It was not known at the time of filing that virus administered to a surgical bed could travel through the lymphatic system to destroy metastatic cells and thus, there would have been no motivation, based on Fong, to use such an approach to treat subjects with tumors found to have metastasized or tumors having a high propensity to metastasize (Applicant's emphasis, Applicant's response, page 10, 2<sup>nd</sup> parag. under "Rejections under 35 U.S.C. § 103(a)"). In response, claim 1, as written, is broad and is not specific for patients with lymphatic metastatic cancer. In addition to this, as

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indicated in the Office Action, February 12, 2007, page 9, "treating" is a broad term and encompasses patients who undergo treatment to reduce or prevent the possibility of having metastatic cancer following resection. As such, Fong et al.'s indication that virus is added to the site of resection to destroy remaining cancer cells is obvious over claim 1.

Thus, the rejection of claims 1, 6, 7 remains.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-6, 8, 9, 28 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kooby et al., 1999, FASEB J. 13: 1325-1334, in view of Rodgers and McCall, 2000, British Journal of Surgery, 87: 1142-1155, for reasons of record, February 12, 2007.

Applicant's arguments filed May 14, 2007 have been fully considered but they are not persuasive.

Applicant indicates that the focus of Kooby with respect to liver metastases of colon cancer is administration of herpes virus by infusion, which results in the virus being delivered throughout the liver. Kooby provides no suggestion or motivation to apply virus to the site of resection. Further, when mentioning the possibility of using the

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approach in conjunction with surgical resection, Kooby notes that the treatment is to reduce local recurrence (citation from Kooby, page 1332; Applicant's response, page 12). In response, this is not persuasive. Regardless of what Kooby et al.'s motivation was for combining virus and resection of the liver (i.e., to reduce postoperative local recurrence, Kooby et al., page 1332, 2<sup>nd</sup> col., 1<sup>st</sup> parag.), Kooby et al. teach the steps of the claimed invention: resection of tumor and administration of virus and thus, Kooby et al.'s teaching is obvious over the claimed invention. Applicant indicates that Kooby et al. do not teach "site of resection," as Kooby et al. teach portal infusion of the viral vector. In response, the phrase, "site of surgical resection" is broad. In addition to phrase being interpreted as, "virus that is directly administered at the site of resection," "site of resection" could also be interpreted as, "in the vicinity of" or "within the same organ." A search of the specification does not provide a specific definition for the phrase, "site of resection," to be limited to direct administration of virus at the site of resection. As such, removal of tumors from the liver and administration of virus via the portal vein, wherein the virus is distributed throughout the liver and eventually reaches the sites of resected tumor, is readable on the claims.

As a reminder, Rodgers and McCall was used to illustrate that metastatic cancer in the liver will also have metastases in the hepatic lymph nodes.

Thus, the claims remain rejected.

### ***Conclusion***

No claims allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

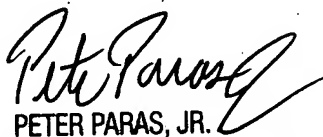
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance.

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Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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Art Unit 1632

  
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